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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/542,769	03/06/2006	Daniel Butzke	WEICKM-0046	5398

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1652	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/542,769	BUTZKE ET AL.	
	Examiner	Art Unit	
	Mohammad Meah	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☐ Claim(s) *1,54,55,64,65,67 and 68* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1, 54-55, 64-65, 67-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claims 1, 51-57 and 64-67 were examined in the previous action. With supplemental amendment of this application, the applicant, on dates 5/14/07, cancelled claims 2-50 and 66 and amended claims 1, 54-55, 64-65 and 67-68. As amended claim 68 is within the scope of the elected invention and therefore is examined herewith. Claims 58-63, 69-104 remain withdrawn as drawn to non-elected invention.

Priority

Acknowledgement is made of applicant's PCT priority date based on application filing date of 01/20/2004 of PCT/EP04/00423 and foreign applications European patent office, EPO 03001232.2 filed on date 01/20/2003, European patent office, EPO 03026613.4 filed on date 11/19/2003.

Objections

Objection of claims 1, 51-57 and 64-65, 67-68 still remain as these claims must be restricted to elected subject matter only, which is isolated polypeptide comprising the amino acid sequence of SEQ ID NO: 2. Applicants argument that if polypeptide of group I is allowable then Group 19, Claims 83-92, method of modulating the activity of target substance or screening target substance using polypeptide comprising the amino acid sequence of SEQ ID NO: 2 is rejoinable is noted however, the objection to claims 1, 51-57 and 64-65, 67-68 as including non-elected subject maters is distinct from the restriction between groups 1 and 19. The objection refers to the continued inclusion of the subject matter of groups 2 and 3 of the restriction requirement in the instant claims. This subject matter is not rejoinable with group 1 upon allowance of group 1 as it recites

distinct products from the product of group 1. The objection will be maintained until applicants cancel the non-elected subject matter.

Claim Rejections

35 U.S.C 112 Rejection

USC 112 2nd Paragraph rejection:

> The following is a quotation of the second paragraph of 35 U.S.C. 112:
> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Rejection of claims 54-55, 64-68 under 35 U.S.C. 112, second paragraph is withdrawn after amendments of the claims.

35 U.S.C 112 1ST paragraph Rejections

Written Description requirement Rejections:

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 55-57 and 64-65, 67-68 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 1 64-65, and 67-68 are directed to a genus of polypeptide molecules comprising either SEQ ID NO:2 or fragments thereof or any polypeptide which is at least 90% sequence

identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising the said polypeptides. The specification does not contain any disclosure of the function of all the polypeptides in said genera. The genus of polypeptides that comprise these above amino acid sequences is a large variable genus comprising many different proteins. Therefore, many functionally unrelated proteins are encompassed within the scope of these claims, including partial amino acid sequences. The specification discloses only a few species of **L-amino acid oxidase from *Aplysia punctata*** of the claimed genus (SEQ ID NOs: 2, 4, 6), which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Therefore, one skilled in the art cannot reasonably conclude that the applicant had possession of the claimed invention at the time the instant application was filed.

Claims 51-55 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. These claims are directed to any oxidase comprising any fragment of SEQ ID NO:2. The genus of polypeptides claimed is a large variable genus with the potentiality of encoding many different oxidases. Therefore, many structurally distinct polypeptides having oxidase activity are encompassed within the scope of these claims. The specification teaches the structure of only a few representative species of such protein (SEQ ID Nos 2, 4 or 6) .which is insufficient to put one of skill in the art in possession of the attributes and features of all species within the claimed genus. Moreover, the specification fails to describe any other representative species by any identifying characteristics or properties

other than the functionality of encoding a protein having amino acid oxidase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Claims 65-65 and 67 are directed to a pharmaceutical composition or kit comprising any L-amino acid that modulates cytotoxic activity of any variant of SEQ ID NO:2. The specification fails describe how any L-amino acid can modulate any polypeptide. The specification discloses only L-lysine and L-arginine modulate l-amino acid oxidase comprising SEQ ID Nos 2, 4 or 6, isolated from *Aplysia* ***punctata*** . L-amino acids are diverse in their structures and modulation of activities of l-amino acid oxidase depends both on the structure of L-amino acid and L-amino acid oxidase. Instant claims comprise modulation of any protein (having no structural limitation). Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Applicants argument against 112 written description rejection, described on their amendment pages 11-13, is considered but not found persuasive because although the specification teaches few amino acid oxidases (SEQ ID NO: 2, 4, 6) from *Aplysia*

punctata, and modulating them with L-lysine or L-arginine, these claims encompass many polypeptides some without sufficient function (claim 1, 56, 57, 64, 65, 67, and 6 claims dependent on it) and some having amino acid oxidase activity without any sufficient structure to provide said oxidase activity (claims 51-55) from any source. Biochemistry of L-amino acid oxidase is known. However knowledge biological function is dependent on sufficient structural knowledge of the bimolecule (Wristlock et al.) . However as explained above and below these claim comprise any polypeptide, or any oxidase and modulation of any protein or any oxidase by any L-amino acid. Such as claims 1, 56-57 and 64, 65, 67-68 encompass any polypeptide molecules comprising any fragment of SEQ ID NO:2 which comprise many polypeptides having any function. Claims 51-55 encompass any polypeptide comprising any fragment of SEQ ID NO: 2 having any oxidase activity. Claims 65-65, 67 are directed to a pharmaceutical composition or kit comprising any L-amino acid that modulates cytotoxic activity of any variant of SEQ ID NO:2 (which comprise any polypeptide having any function.). The genera of polypeptide recited in the claims is a large variable genus that applicant do not teach how all these diverse polypeptides will have recited function or do not teach sufficient structure to provide the recited function as many fragments of SEQ ID NO:2 lack any oxidase activity. Given this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention.

Enablement Rejections

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1, 51-57 and 64-65,67-68 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the L-amino acid oxidase of SEQ ID NO:2, or pharmaceutical kit comprising said amino acid oxidase and L-amino acid as modulator, does not reasonably provide enablement for any polypeptide molecules comprising any fragment of SEQ ID NO:2 or any L-amino acid oxidase which is at least 90% sequence identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising said polypeptides. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, make and for use the invention commensurate in scope with these claims.

Claims 1, 56-57 and 64, 65, 67-68 are so broad as to encompass any polypeptide molecules comprising any fragment of SEQ ID NO:2 or any L-amino acid oxidase which is at least 90% sequence identical to the polypeptide of SEQ ID NO: 2 or pharmaceutical kits comprising the said polypeptides. Claims 51-55 are so broad as to encompass any polypeptide comprising any fragment of SEQ ID NO: 2 or any polypeptide which is at least 90% sequence identical to the polypeptide of SEQ ID NO: 2, wherein said polypeptide has amino acid oxidase activity or pharmaceutical kits comprising the said polypeptides and L-amino acid. The scope of the claims is not

commensurate with the enablement provided by the disclosure with regard to the extremely large number polypeptide molecules broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the amino acid sequences of only a few amino acid oxidases (SEQ ID Nos: 2, 4 and 6).

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable (e.g., Whisstock, et al. Quarterly Rev. Biophy. 2003, 36, pp 307-340). In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims 1, 51-57, 64-68 which encompass any protein having 90% identity to SEQ ID NO: 2 because the specification does **not** establish: (A) regions of the protein structure which may be modified without effecting amino acid oxidase activity; (B) the general tolerance of

amino acid oxidase to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid oxidase residues with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any polypeptide with an enormous number of modifications of amino acid residues of a protein having amino acid sequence of SEQ ID NO: 2. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of amino acid oxidase polypeptide, having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants arguments against rejection of the claims under 35 USC 112 first paragraph enablement requirement are acknowledged but not found persuasive as explained above. Although the specification is enabling for the polypeptide of SEQ ID NO: 2 or a protein having 95% sequence identity with SEQ ID NO:2 having oxidase activity, does not reasonably provide enablement for any polypeptide molecules having 90% SEQ ID NO: 2 or any fragment thereof described in the claims. Because as explained in prior rejection and also above the genus of polypeptide claimed in the instant claims are broad variants of polypeptide that specification do not describe. To find out which polypeptide among these enormous number of polypeptides molecules

that have said oxidase activity would be required the necessity of producing and testing all of the virtually infinite possibilities. This would clearly constitute **undue** experimentation. While enablement is not precluded by the necessity for routine screening, if a large amount of screening is required, the specification must provide a reasonable amount of guidance with respect to the direction in which the experimentation should proceed. Such guidance has **not** been provided in the instant specification. Examiner acknowledge the omission of sending Wisstock et al reference to the applicant and it will be send herewith. However applicant's argument against it use in enablement rejection is not found persuasive as explained above applicants claims a broad class of polypeptides some having undefined structure and some having undefined function.

CLAIM Rejection - 35 U.S.C 102

35 U.S.C 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Rejection of claims 1, 51-57, 64 under 35 U.S.C. 102(b) as being anticipated by Isaac et al. (US pat 6372211) remain. Isaac et al. teach a L-lysine oxidase, comprising residues 120-135 of SEQ ID NO: 2.

Applicant argument that Isaac et al. does not teach a structure comprising SEQ ID NO: 2 is found to be true but applicant's claims recite L-

amino acid oxidase which comprise any fragment of SEQ ID NO: 2 which is taught by Isaac et al. Therefore Isaac et al. anticipates applicants claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed M. Y. Meah whose telephone number is 571-272-1261. The examiner can normally be reached on 8:30-5PM.If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 571-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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